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TITLE: Advanced Pediatric Brain Imaging Research and Training Program

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CONTRACTING ORGANIZATION: Children's National Medical Center
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14. ABSTRACT

Brain injury is a leading cause of death and disability in children. Recent advances in pediatric magnetic resonance imaging (MRI) techniques are revolutionizing our understanding of brain injury, its potential for recovery, and demonstrating enormous potential for advancing the field of neuroprotection. We have created a highly structured, collaborative, and multidisciplinary training program in **BRAIN** (**B**rain **R**esearch **A**dvanced **I**maging with **N**MR) to advance research skills of investigators from all branches of the US military focusing on pediatric brain injury. Our goal is to train, with the highest rigor, military trainees in conducting clinical research using advanced brain imaging technologies to study the causes and consequences of pediatric brain injury. Over the past year, we successfully implemented the on-site BRAIN training curriculum. We recruited two military trainees in year 1 [2012-2013] and a civilian trainee in year 2 [2013-2014]. In order to circumvent the current challenges associated with military trainee recruitment and retainment in the BRAIN program, secondary to the sequestration, over the next year, we plan to develop and implement a web-based BRAIN curriculum that will be made available to DoD and civilian trainees undergoing their clinical rotations at Children's National. Thereafter, the BRAIN curriculum will be deployed externally and exclusively on-line to all major DoD military bases. This will allow a more broad-based teaching framework in which we anticipate far-reaching benefits including a major increase in reach of the program while mitigating the need for travel.

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INTRODUCTION

The overarching objective of this grant is to advance the training of military clinician scientists in the field of investigative neuroimaging techniques that are revolutionizing our understanding of brain injury, its recovery after injury, and demonstrating enormous potential for advancing the field of neuroprotection and neurorehabilitation.[1-6] Our **BRAIN** (**B**rain **R**esearch **A**dvanced **I**maging with **N**uclear Magnetic Resonance) program is created under the hospice of three goals which focus on developing (i) the scientific rigor necessary to perform high-quality clinical research through instruction in epidemiology and biostatistics, (ii) an in-depth understanding of the underlying pathogenetic mechanisms of injury to the brain and its recovery, and (iii) the necessary skills to apply advanced MRI techniques to specific clinical research questions. The long term goal of this training program is for military clinician scientists to apply reliable, state-of-the-art, and clinically useful advanced brain imaging techniques to facilitate the diagnosis, management, and ultimately treatment of brain injury.

BODY

In July 2012, we successfully recruited two high-caliber military trainees who began their training in BRAIN. Dr. Gerald E. York, our first research scholar was a neuroradiologist from Brooke Army Medical Center (BAMC) in Houston, Texas. Our second scholar, Dr. Nicole Dobson was a neonatologist at Walter Reed Army Medical Center from Uniformed Services University in Bethesda Maryland. Dr. York's project focused on the application of serial, quantitative MRI techniques to characterize structural, functional, and metabolic changes following mild traumatic brain injury in children. Dr. Dobson's project was an investigation of the mechanisms of brain injury in premature infants, and potential neuroprotective effects of caffeine. The BRAIN curriculum was successfully implemented in which Drs. York and Dobson actively participated in. The trainees also benefited from hands-on training in advanced image post-processing supported by our MRI training cores (described below).

Regrettably, Dr. Dobson's unexpectedly decided to discontinue her training in BRAIN in November 2012 for reasons related to a change in her career plans. Dr. York made significant progress in the data acquisition and MRI processing phases of his research study while actively immersed in the BRAIN training program at Children's National. However, his progress was unexpectedly, and prematurely arrested as a result of a military travel moratorium that ensued the end of 2012, related to sequestration. Moreover, in order for Drs. Dobson and York to participate in BRAIN, we were required to establish agreements with their home institutions. Children's National executed an agreement with National Capital Consortium permitting Dr. Dobson to participate in the BRAIN program at Children's National in July 2012. Unfortunately, we were not able to enter into an agreement with Dr. York's home institution [previously described in semi-annual progress report (Appendix 1) and Dr. Tibbetts' letter (Appendix 2)].

We proceeded to bring together our external advisory committee for a site visit on April 18, 2013, at which time progress and obstacles were presented. The committee's overall evaluation of the program was excellent and their recommendations were two-fold: i) to incorporate distance learning solutions given the success of the BRAIN curriculum, and ii) the inclusion of civilian trainees while the PI and program directors work towards identifying solutions to the challenges currently facing military trainees (Appendix 3). We also met with Dr. Melissa Forsythe (Program Officer) on May 9, 2013 to discuss the barriers that had impeded our progress to date, and the challenges faced in recruiting and sustaining prospective military trainees. On July 1, 2013, we received approval from Dr. Forsythe to restructure and broaden the scope of our BRAIN training program.

Rationale for expansion of the BRAIN Program to a web-base model for remote learning. We are proposinf a change in the approach to meeting the fundamental training goals of the BRAIN program, i.e., clinical research design and implementation, the pathophysiology of brain injury and recovery, and the use of quantitative MRI techniques for addressing future research questions. The essence of our proposed change in the program regards the training medium from the individual on-site training model, to a web-based model for remote learning. This change is necessitated by the unexpected developments described above including the US economy, the sequester and a resulting travel moratorium for DoD members. However, we anticipate far-reaching benefits from this web-based distance-learning tool. Some of these include 1) a major increase in reach of the program; 2) obviating the need for travel; and 3) time-flexibility for trainees that relocate between military bases, even deployment to remote regions of the globe. We elaborate on these benefits below.

In addition, we envision this revised plan as a pilot program for a more expanded program in continuing medical education for multidisciplinary pediatric and, later, adult medicine training. It is important to note that although the current proposal is for a pediatric brain-oriented program, our goal is to demonstrate success and then to submit proposals for expansion of the program to include: i) The Brain Across the Lifespan, and subsequently, and 2) Other specialties of relevance to the DoD, essentially aiming for a comprehensive multidisciplinary site for ongoing medical education. Over and above the remote learning impact, such a portal could also serve as an interactive training site with the necessary flexibility for break-out subject teaching relevant to the constantly evolving challenges facing the US military medical corps. The development of this tool as a portal for collaborative clinical research would include the standardized training of multicenter teams, sharing of data, centralized biomedical expertise and data processing. Ultimately such a tool could serve as a repository for large collections of recorded physiologic signals and related open-source software accessible to the military for research and development. With successful implementation of the web-based architecture described below the modular expansion of subject matter proposed should be relatively easy. The revised budget is being finalized and will be provided to our Program Officer in a separate document.

Finally, as per the original approved grant, we have recruited a civilian trainee in which we had approval to include one civilian trainee in years 1 and 2 of the grant. In year 1, we did not recruit any civilian trainees as we identified and recruited two very strong military trainees. Over the past year, the success of the program among civilian trainees stimulated great interest, and we were fortunate to recruit a high-caliber civilian trainee for the upcoming year (**Dr. An**

Massaro, a neonatologist at Children's National Medical Center), who started in the BRAIN program in September 2013. Dr. Massaro's research project in BRAIN is described below.

Statement of work – progress to date:

Specific Aim 1: To advance the understanding of the fundamental principles and clinical application of sophisticated MRI techniques that is revolutionizing clinical research into the causes, consequences and care of pediatric brain injury.

Over the past year, the PI together with the scholarly oversight committee successfully implemented clinical teaching seminars on the fundamental principles and applications of advanced MRI techniques (Appendix 4). The program has compiled a diverse team of scientists with a remarkable depth and breadth of expertise. Particularly gratifying has been the growth and accumulating expertise behind the seminar series, which are attended to maximum capacity, as well as the confluence of multidisciplinary expertise. The program demonstrated significant training benefits not only for the recruited military trainees but for our civilian trainees and junior faculty across multiple specialties including fetal medicine, neonatology, neurology, critical care medicine, radiology, biomedical engineering, cardiology nursing, psychiatry and psychology. Given that Dr. York was unable to continue his training on site following the military travel moratorium, we organized remote video conferencing capabilities to allow Dr. York to continue to participate in these seminars.

We also developed a core curriculum of hands-on training sessions in quantitative MRI techniques through our MRI and Neurobehavioral training cores which were fully operational over the past year. Available to our trainees were five imaging training cores including MR spectroscopy, Diffusion MRI, Perfusion MRI, Morphometric MRI and Functional MRI training cores with designated lead mentors for each core by our CNMC-NIH team of investigators. In these hands-on sessions, our trainees were guided in the application of advanced software tools that enable quantitative measurements offered through a large repository of imaging modalities including brain volumetric and cortical surface measures, brain diffusion, perfusion, metabolic and functional metrics. **Dr. York** was able to complete a proportion of his MRI data processing while on-site at Children's National, and was focusing on analyzing the longitudinal structural evolution of changes in specific brain tissue volumes over the course of recovery from TBI in order to quantify cortical sulcal volumes, cortical gray matter thickness, and white matter volume alternations. Upon completion of the image processing of his volumetric data (within the

Brain Morphometry Training Core), he began a rotation at Dr. Pierpaoli's laboratory at the NIH (co-Investigator on the grant, and Lead mentor for Diffusion Tensor Training Core). Dr. York was near completion in his processing of brain microstructural (DTI) data, which would lead to analysis of longitudinal changes in white matter fiber track architecture after TBI. Dr. York was planning to submit these preliminary data as an abstract to the international Human Brain Mapping meeting but the plans were derailed (as detailed above). The next critical phase of his work was supposed to focus on completing the structural analyses and relating these to the clinical and neuropsychological outcomes of his subjects. Unfortunately, he was unable to return to Children's National to complete his data analysis. Despite this major set-back, Dr. York was able to use the skills he acquired while training in BRAIN and was awarded an extramural grant and participated in a number of scholarly meetings over the past year (described under Reportable Outcomes section).

Drs. York and Dobson also benefited from our Neurocognitive core which provided teaching on developmental, cognitive, and behavioral outcomes for children who have suffered brain injury. The neurocognitive training core exposed trainees to the role of neuropsychological and neurobehavioral testing. The DoD trainees, and our civilian trainee (Dr. An Massaro) successfully completed the Pediatric Neuropsychology Training Day which covered a number of topics includes neurodevelopmental principles, functional neuroanatomy, and the role of neurocognitive testing in assessing structure-function relationships.

Dr. Massaro, our current civilian trainee have been actively developing her clinical research project that will incorporate advanced MRI techniques to study hypoxic ischemic brain injury in newborns treated with therapeutic hypothermia. Dr. Massaro has a long standing interest in identifying early biomarkers of brain injury and improving outcome in patients with hypothermia-treated neonatal encephalopathy. In the context of a prospective, longitudinal cohort study, Dr. Massaro's project will focus on the application of serial and quantitative MRI techniques to examine the microstructural and perfusion consequences following neonatal hypoxic ischemic encephalopathy. Neurodevelopmental outcomes will be correlated with the proposed quantitative MRI measurements. This work will be conducted under the mentorship of Dr. Catherine Limperopoulos (PI), Dr. Adre du Plessis (co-investigator and Associate Director of BRAIN), Dr. Iordanis Evangelou (co-investigator and perfusion MR training core lead) and Dr. Carlo Pierpaoli (co-investigator and diffusion MR training core lead). The next phase of her training will include hands-on application of advanced MRI techniques to analyze diffusion tensor imaging and perfusion (arterial spin labeling) MRI data and to relate measures of global and regional brain microstructural organization and perfusion to neurodevelopmental outcomes.

Dr. Massaro will analyze her data and prepare her manuscripts. Her long-term goal is to apply the advanced pediatric brain imaging techniques she will acquire during her training in BRAIN to submit for grant funding to study reliable imaging biomarkers of evolving brain injury that will guide rational therapeutic decision-making in neonatal hypoxic ischemic encephalopathy.

Specific Aim 2: To enhance through didactic and clinical teaching the basic science and clinical understanding of the causes, mechanisms, and consequences of pediatric brain injury.

Over the last year, significant progress was also made in the teaching seminars on the Principles of Pediatric Brain Injury which take place alongside, seminars in Advanced Brain Imaging Techniques described in specific aim 1.These teaching seminars have become an extremely valued academic series at Children's National with increasing attendance at standing room only capacity. The lectures encompass a broad spectrum of acquire forms of brain injury, including hypoxia-ischemia/reperfusion, hemorrhage, trauma, metabolic, and others (Appendix 4). In these lectures a direct connection is made between breakthroughs in basic/experimental neuroscience and specific features of a 'toolbox' of established and emerging quantitative MRI methods available to clinicians (described in Aim 1). As described in specific aim 1, we were successful in setting up videoconferencing access to our BRAIN lectures for Dr. York (following the travel moratorium that was instituted late 2012), in order for him to continue to benefit from the BRAIN curriculum academic activities.

Specific Aim 3: To provide training in clinical research methodology through courses and seminars in biostatistics and research design, and responsible conduct of clinical investigation.

Drs. York and Dobson successfully completed a two-week intensive course on Introduction to Clinical Research at Johns Hopkins University. Unfortunately, Dr. Massaro did not have the opportunity to register for this course given that advanced registration in the spring was required in order to participate in the program in early July. At the time, approval from Dr. Forsythe regarding restructuring the program was pending. However, Dr. Massaro has previously completed a clinical research training consortium program and is currently participating in the **C**hildren's **R**esearch **E**ducation **A**nd Career **T**raining (CREAT) Program at Children's National Medical Center. All trainees (Drs. York, Dobson, and Massaro) successfully completed the on-

line Collaborative Institutional Training Initiative (CITI) course on responsible conduct of research. Similarly, all trainees developed their research projects and obtained IRB approval (For Drs. Dobson and York, this was described in detail in the first Annual Report, October 2012). Currently, Dr. Massaro has also been actively developing her research projects (describe in aim 1) which will take place at Children's National and is entitled, Predicting Outcomes in Patients with Hypothermia-Treated neonatal Encephalopathy (Pro#00000216, An Massaro, PI).

Development of a Remote BRAIN curriculum

To achieve the specific aims set forth in the original statement of work (described above) and make the BRAIN curriculum more broad-based, we will develop a secure, web-based learning portal system. The online training will be housed in a web-based learning portal (*Appendix 5*). The custom BRAIN training portal site is envisioned to be a single-point of access that military and civilian medical professionals can search, upload, and house online training and education-related information. The site will be modular with various databases, ranging from simple to complex, and the latest features such as computer-based trainers, learning and communication widgets and plug-ins, and external instructional and productivity tools. Additionally, the site will be secure allowing users to login as members or guests. Permissions are assigned by the administrator to each user account (e.g. *user, site creator, manager or administrator*). There will be a self-registration feature to handle large numbers of users wanting access to the system. The main dashboard will display courses a learner is enrolled in, and can be displayed or hidden from public viewing. Instructors can customize a course by activating the edit feature and populate it with built-in educational resources and activities can be easily added or removed to suit a learner's needs. The calendar feature allows users to view assignments and activities at the site-level.

We have been fortunate to recruit Mr. Jeff Sestokas who is a Senior Instructional Systems Designer and Research Scientist at Children's National Medical Center specializing in the application and diffusion of instructional technologies to military and corporate firms. Prior to working at Children's National, Mr. Sestokas was a Senior Scientist at Engineering and Computer Simulations and Applied Research Associates. Over the years, he has worked on projects developing training for complex, multi-agency and military command environments with a focus on designing scenarios, evaluation, and assessment tools within computerized and live environments. He has authored and co-authored several publications on topics relating to instructional design and technology. He received his M.A. Ed. in Instructional Design and

Technology and a B.A. in English focusing in secondary integrated language arts from Baldwin-Wallace College. As can be seen from his CV (Appendix 6) he has the skills and experience to achieve the web-based remote-learning goals set out in the revised protocol.

Design Plan: During the design phase lum, our primary objective will be to design online courseware based on the seminar series we have already developed, that will train DoD and civilian medical professionals in in the principles and clinical applications of advanced MRI and basic mechanisms of brain injury and recovery, and clinical research methodology. To achieve this goal, we will use a used a five–step design approach that focuses on designing content that incorporates learning outcomes, learner abilities, instructional methods, instructional content, and assessment methods (Appendix 7).

Implementation Plan. The following sections describe our initial implementation plan. We will modify this plan according to the research findings and guidance from our DoD sponsors to produce a final implementation plan. This implementation plan poses topics and describes activities for successfully fielding instructional technology-based tools built for the DoD and civilian medical community. To begin, we provide suggested high-level objectives and strategies for achievement that help focus our efforts in implementing technology-based platforms and educational tools within different user populations.
These objectives include:

- Promoting a Custom Online BRAIN Learning Portal (*i.e. brain injury training content management platform and training resources*) and its benefits (*e.g. learning improvement, job efficiency, and cost reduction*)
- Implementing short- and long-term marketing and sustainment strategies such as:
    - Organizational acceptance through:
        - Endorsements from internal and external medical groups and associations
        - Creating and implementing outreach activities
        - Writing publications
    - Technical assistance using:
        - Help desk staff for troubleshooting
        - Annual step-by-step user guides
    - Training support by preparing:
        - Training workshops
        - Annual facilitation guides

- Long-term system sustainment including:
    - Hosting (shared vs. dedicated)
    - Instructional technology staff support for new customizations

➢ Encouraging user assessment of training portal and educational tools through:

- Further research
- Additional test and evaluation via:
    - Surveys
    - Questionnaires

Implementation Activities. As mentioned above, a primary goal of this proposal is to lay out strategically the strategy for integrating educational and technology-based products by actively promoting awareness and informing target audiences throughout the development life-cycle. The seminars that were developed originally (Appendix 4) will be used to implement a custom online brain injury training portal and supplemental educational activities.

Organizational Acceptance. For Children's National to implement an online BRAIN training portal into practice, the site must first be accepted by key Government and military stakeholders as an applicable tool for providing distance learning, enhancing online collaboration, and training/exercising brain injury education in real world contexts. A mechanism for encouraging organizational buy-in is to inform and obtain upper-level leadership support at both executive and ground floor levels. We will do this by demonstrating that the portal and associated educational tools save time and training costs, and provide quality training experiences.

Technical Assistance. Another area for consideration when implementing an online training portal is to provide technical support to assist users in problems or challenges that may arise when operating the software. In general, technical support services will attempt to help users solve specific problems with the portal rather than providing training, customization, or other support services. Technical support may be delivered over the telephone or online by e-mail, or directly through the website portal via instant messenger where users can report an incident and the call can be logged by the support representative. Annual users guides that illustrate best practices and new features of the tool can also be issued to end user community as a form of technical support.

Training Support. The purpose of training support is to reinforce, maximize, and sustain the capability, capacity, and performance of the training portal for the end user. Training support will

be made available through in-person training systems such as train-the-trainer workshops or through independent references such as coaching or facilitation guides. Facilitation guides can be used to assist medical professionals in user the content management portal tools and resources by providing instruction that specifically concentrates on presenting teaching strategies, expert tips, and best practices for utilizing the tools and resources contained within the portal system.

System Sustainment. For the sustained success of this on-line training portal, updating the hardware and software will be important. A key element to continued use of the system is providing a logistical tail to allow implementation of new features and incorporation of user feedback. Upgrades that address user feedback and evolving needs provide a sense of "ownership" for the user, while a system that doesn't change over time to meet the most frequent user requests will frustrate and eventually alienate the user community. Input for these upgrades and new features come via direct user feedback to the website, after action reviews following training events, and help-desk requests.

User Research. Lastly, to successfully implement an online training portal for brain injury, research should be conducted to document and report the effectiveness and usage of the tool for training and teaching expert clinical decision-making and reasoning strategies. If discrepancies exist between the initial implemental findings identified in the early phases of field testing, we will examine these discrepancies and make design adjustments to the portal platform and/or tools. The output of the follow-up research will be requirements used to enhance the existing portal functionality, document best practices for using the tools, and present learning effectiveness results.

Potential Impediments and Impacts. Lessons learned from implementing online portals and training for corporate and military organizations indicate that a significant impediment to successful adoption of online tools and resources is a reluctance to utilize new technology-based methods for conducting training. One approach to overcoming this reluctance is to provide real-time coaching and facilitation support within the user community. We plan to offer both onsite and webinar facilitation support services to as many interested user populations who wish to participate.

Summary of BRAIN training web-based curriculum. As part of our original proposal we have successfully developed and implemented a comprehensive three-level curriculum in which we combine a high-level understanding of the physiology and pathophysiology of brain injury, the clinical manifestations, and the new opportunities provided by advanced MRI technology for exploring mechanisms of injury and intervention, and providing training in clinical research methodology.

Over the course of the next year we will achieve the following three goals:

1) We will update and upload the BRAIN lecture modules developed during the initial period of DoD funding. This will include the didactic lecture series as well as interactive tutorials demonstrating the programs for advanced MRI quantitation.
2) We will implement the curriculum internally at Children's national making it available to DoD and civilian residents and fellows undergoing their clinical rotations through the institution.
3) We will identify partners in the DoD who will assist in
    a. ensuring that the BRAIN web-site meets DoD security standards;
    b. advertising the web-site to all major DoD sites around the globe

As we develop the web-based BRAIN curriculum, we will support one final trainee over the next year (Dr. An Massaro) within the on-site training program. Once the web-based BRAIN curriculum will be developed internally over the next year, we plan to deploy the curriculum in years 4 and 5 to different military bases.

KEY RESEARCH ACCOMPLISHMENTS

-Successful recruitment of one civilian trainee in the BRAIN training program for 2013-2104 (Dr. An Massaro), and two military trainees in 2012-2013 (Drs. York and Dobson).

-Successful completion of the on-line Collaborative Institutional Training Initiative (CITI) course on responsible conduct of research by all trainees.

-Successful completion of the Pediatric Neuropsychology Training Day by all trainees.

-Mentoring teams for all trainees were previously (Drs. York and Dobson) and are currently established (Dr. Massaro).

-Research project has been developed and Institutional Review Board approvals were/are firmly in place.

-Successful implementation of on-site BRAIN Curriculum.

-Recruitment of Jeff Sestokas to support the development of a web-based BRAIN curriculum.

REPORTABLE OUTCOMES

Academic Presentations

Dr. York presented a lecture at the Center for Neuroscience and Regenerative Medicine at the National Institutes of Health Research entitled, “Magnetic Resonance Spectroscopy and Traumatic Brain Injury” (November 2012)

Dr. York presented on “Advanced Brain Imaging in the Emergency Room” to the American Society of Emergency Radiology (October 2012).

Dr. York presented: “Army Traumatic Brain Injury Imaging Initiative” to the Commander of the Medical Corp. (May 2013).

Grant submissions

Dr. York was awarded a 2-year grant by the Center for Neuroscience and Regenerative Medicine ($300,000). “Evaluating plasticity using diffusion tensor imaging in a traumatic brain injured population undergoing cognitive therapy”.

Other Outcomes

Dr. York was invited to be a member of the research committee of the American College of Radiology Head Injury Institute (2013)

CONCLUSION

In summary, we have successfully developed and implemented an innovative, multidisciplinary on-site BRAIN teaching curriculum at Children's National Medical Center. However, in order to circumvent the current challenges associated with recruiting and retaining military trainee engagement in BRAIN training, over the course of the next year, we will implement a web-based learning curriculum that will be developed and field tested internally at Children's National. The curriculum will be made available to DoD and civilian residents and fellows undergoing their clinical rotations through the institution. In parallel, we will train on last trainee (Dr. An Massaro) who will benefit from the already established on-site BRAIN training program. Thereafter, the BRAIN curriculum will be deployed externally and exclusively on-line to all major DoD military bases. This will allow a more broad-based teaching framework in which we anticipate far-reaching benefits including a major increase in reach of the program while mitigating the need for travel; and increased flexibility which is critical for military trainees that relocate between military bases.

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APPENDICES

Appendix 1 Semi-Annual Progress Report

Appendix 2 Dr. Tibbetts letter

Appendix 3 External Advisory Committee Report

Appendix 4 BRAIN Seminars

Appendix 5 Example of a Medical-based Online Learning Portal

Appendix 6 Jeff Sestokas: Curriculum Vitae

Appendix 7 Five-step Design Approach for Developing the Online Brain Courseware

Cover Page

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Section I - A brief introduction covering the purpose and scope of the research effort

The focus of this grant is to advance the training of military clinician scientists in the field of investigative brain imaging techniques. Over the course of the past 18 months, we have developed a highly structured, collaborative, and multidisciplinary training program in **BRAIN** (**B**rain **R**esearch **A**dvanced **I**maging with **N**MR) to advance research skills of investigators from all branches of the US military focusing on pediatric brain injury. The program encompasses (i) didactic training on how to perform high-quality research, (ii) hands-on computational training in quantitative MRI methods, and (iii) the development of a clinical research project under the supervision of a senior researcher team. The overarching *objective* of BRAIN is to train, with the highest rigor, military trainees in conducting clinical research using advanced brain imaging technologies to study the causes and consequences of pediatric brain injury; and translating discoveries, with the goal to assess, treat, and protect the injured brain.

Section II - A brief description of overall progress

IIa) Trainees

Dr. York has made significant progress in the data acquisition and processing phases of his research study, which focuses on the structural and metabolic effects of mild traumatic brain injury (TBI). Specifically, he has processed all the MRI data on his subjects and is analyzing the longitudinal structural evolution of changes in specific brain tissue volumes over the course of recovery from TBI. These data will permit analysis of cortical sulcal volumes, cortical gray matter thickness, and white matter volume changes using the patient's initial scan as a "baseline." Once he completed image processing of his volumetric data, he began a rotation at Dr. Pierpaoli's laboratory at the NIH (co-Investigator on the grant, and Lead mentor for Diffusion Tensor Training Core). He is near completion in his processing of brain microstructural (DTI) data, which will lead to analysis of longitudinal changes in brain fiber track architecture after TBI.

Comparison to the control subject MRI scans will also be performed for the DTI data. Dr. York was planning to submit these preliminary data as an abstract to the international Human Brain Mapping meeting but the plans were derailed (see section III below). The next critical phase of his work will focus on completing the structural analyses and relating these to the clinical and neuropsychological outcomes of his subjects. Dr. York has also been an active participant in the BRAIN teaching curriculum.
Dr. York has also presented a lecture to the CNRM group at the NIH that reviewed the application of ^{1}H-MRS to the study of TBI.

Dr. Dobson's research was an investigation of the mechanisms of injury to the developing brain and potential neuroprotective strategies in premature infants. Unfortunately, she unexpectedly decided to discontinue her training in the program for reasons related to a change in her career plans. Prior to resigning, she had defined a research project that examined the potential neuroprotective effects of caffeine on the preterm brain, using advanced brain imaging techniques. She had assembled a dedicated mentorship team of Dr. Catherine Limperopoulos (PI; MRI morphometry training core lead), Dr. Adre du Plessis (co-investigator and Associate Director of BRAIN), and Dr. Carlo Pierpaoli (co-investigator and diffusion MR training core lead). Dr. Dobson had also started hands-on training in the application of advanced MRI techniques. Her leaving is regrettable on a number of fronts including the amount of time and effort spent in coordinating her team and studies.

IIb) BRAIN Curriculum

Teaching seminars on the Principles of Pediatric Brain Injury (Dr. Adre du Plessis) and Advanced Brain Imaging (Dr. Raymond Sze) have become a highly valued event in the academic calendar of Children's National Medical Center with a growing attendance currently at a standing room only capacity. We have also set up remote video conferencing capabilities to allow Dr. York and others to

participate in these seminars when they are off-site. This is a capability in which we would like to expand in future.

Section III - Problem Areas

(a) A description of current problems that may impede performance along with proposed corrective action.

In order for Drs. Dobson and York to begin their training in BRAIN, we were required to establish agreements with their home institutions (Walter Reed Army Medical Center [Dr. Dobson] and the Brooke Army Medical Center [Dr. York]). Children's National executed an agreement with National Capital Consortium permitting Dr. Dobson to participate in the BRAIN program at Children's National in July 2012. Unfortunately, Children's National was not able to enter into an agreement with the U.S. Government permitting Dr. York's participation in this same program despite the fact that Children's National remained available to comply with the contract terms and other legal terms required for Dr. York's participation. See also attached letter from Dr. Tibbetts (Chief of Radiology, BAMC). We understand that this may have been due to a military instituted travel moratorium in late 2012, but request that you please contact the U.S. Military directly to confirm this.

(b) Anticipated problems with potential to impede progress and proposed corrective actions.

In addition to the unresolved issues above, several problem areas are likely to impede progress. The lack of a designated contact within the military to help us navigate issues on the military side of this agreement will continue to impede progress. Directly related to this issue are the challenges faced by the Children's National Medical Center investigators in advertising BRAIN, screening applicants, and recruiting trainees. Proposed corrective actions would be to request that the military designate an appropriately informed official who would help expedite communication between the military and CNMC. This person should have the understanding of the military GME regulations, policies and

procedures appropriate to facilitating the participation of U.S. Military in external programs such as BRAIN. In addition, assistance from the U.S. Department of Defense as to the optimal means for advertising BRAIN among military clinician-scientists, thereby facilitating the recruitment process of prospective trainees, would be helpful as well.

Section IV - Work to be performed during the next reporting period.

In the next period we will organize our external advisory committee meeting during which progress and challenges encountered over the past 6 months will be reviewed. In addition, we plan to continue developing our capabilities for remote teaching through our videoconferencing system. To date this has been successful in keeping Dr. York actively involved with our group. This approach also has enormous potential for allowing us to transmit our current and future BRAIN curricula to interested clinician scientists in the military.

Section V - Administrative Comments (Optional)

Dr. York hopes to return to CNMC to complete his analyses, which should lead soon thereafter to the first of several publications.

DEPARTMENT OF THE ARMY
BROOKE ARMY MEDICAL CENTER
3851 ROGER BROOKE DRIVE
JBSA FORT SAM HOUSTON, TEXAS 78234-6200

March 12, 2013

Department of Radiology

Children's National Medical Center
ATTN: Dr. Limperopoulos
Washington D.C.

Dear Dr. Limperopoulos,

I wanted to write you w/ some explanation of the difficulties faced in sustaining an agreement with your facility.

In every way, the idea of pursuing a relationship for experience in pediatric neuroimaging and image analysis towards research collaboration and strength within MTFs is one we really liked. Indeed, we hoped to help model how that might flow to improve your opportunities at securing physicians with whom you could collaborate at other MTFs.

We worked through a number of early snags/resistance or thought we had to include the legality of the agreement. I included our graduate medical education office in the planning and construct of the formal agreement because of both their expertise and to clarify that from DOD GME perspective this was not to be considered a fellowship. GME programs have very specific criteria for a selection board and a long lead time. Both that process and the modified agreement we made with you did not seem to fit that mold. Indeed, because you intend trainees to return and collaborate with you on nascent research opportunities at their origin MTF, the DOD GME process fails to guarantee that. A residency or fellowship is by nature a permanent change of station which on completion leads to a new assignment with no guarantee of return to the same facility, compromising the expectations of follow-up in the planned second year.

Our agreement had passed scrutiny at several levels and it seemed quite reasonable to us that final approval was only a formality, so I allowed Dr. York to begin with you in a permissive travel status (un-reimbursed) so as not to miss key early training opportunities. A number of surprises followed including detailed enquiries at the commanding general level and re-questioning of higher authorities in command, legal and GME areas of expertise. It only took one of these to view the selection process and agreement with skepticism, slowing approval to a crawl, while hoping to find a distant future way forward. As we sought reconsideration, budget crises loomed and the belt-tightening caused any roles for clinical personnel outside of care and the generation of RVU's to be suspect.

A deeper financial crisis only added more nails to that closed door.

I do not see a secure way forward for the program as written in the grant. While no expert on the legal avenues and GME policy, it seems to me that the Military Health System has only one means of formally selecting among candidates and that is our Health Professions Educational Review Board, where applicants are

reviewed, selected and subsequently signed to additional commitment in exchange for GME opportunities. Some organizations within the DOD may have special dispensations to go around these, if they can establish training opportunities as requirements (for example the Defense Veterans Brain Injury Center or Institute for Surgical Research). This would necessarily include a requirement to them and approved tasking through the Surgeons' General.

Outside of such a tasking, the current environment fosters no opportunity for me to foster such long term training opportunities for my staff at distant facilities no matter how attractive the opportunity. Indeed, I have not been able to send a single staff to a CME conference in the current fiscal year, let alone "fund" the absence of a researcher for up to 50% of duty time.

I remain in agreement with the intent and hopes of your program opportunity and the grant under which the offer was extended and can only hope that you are able to find a way forward through other avenues. Should anyone have questions on specifics, or pointers to contacts who may be able to help in the future, they may contact me by phone (210-916-4218) or email (grant.p.tibbetts.mil@mail.mil).

Sincerely,

Grant P. Tibbetts, Colonel, USAF, MC
Chairman, Department of Radiology

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3851 ROGER BROOKE DRIVE
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Sincerely,

Grant P. Tibbetts, Colonel, USAF, MC
Chairman, Department of Radiology

CENTER FOR FUNCTIONAL AND MOLECULAR IMAGING

GEORGETOWN UNIVERSITY MEDICAL CENTER

July 16, 2013

Catherine Limperopoulos, PhD
Director, MRI Research of the Developing Brain
Director, Advanced Pediatric Brain Imaging Research Laboratory
Diagnostic Imaging and Radiology/Fetal and Transitional Medicine
Children's National Medical Center
Associate Professor of Neurology, Radiology, and Pediatrics
George Washington University School of Medicine and Health Sciences
111 Michigan Ave. N.W.
Washington, D.C. 20010

Dear Catherine,

The following is the report regarding the site visit of by the External Advisory Board for your Department of Defense (DoD) training grant entitled "Advanced Pediatric Brain Imaging Research Training Program (W81XWH-11-2-0198)", which met on April 18, 2013. The board members consist of myself and Drs. Michael V. Johnston and Ashok Panigrahy.

Our uniform consensus is that you have formed an excellent training program for DoD trainees in the latest imaging techniques in pediatric brain injury, clinical research, and translation of these techniques to the bedside. The training program is comprehensive and incorporates experts from both Children's National Medical Center and National Institutes of Health. The topics covered in your program include diffusion tensor imaging (DTI), MR spectroscopy (MRS), morphological analyses such as voxel-based morphometry (VBM), and functional MRI (fMRI). The only problem identified was with respect to the numerous hurdles in working with the various branches and components of the military related to obtaining permission for the trainees to attend this training program: release from their current command to attend and the need to avoid incurring additional military service commitment. You and others have made numerous attempts to overcome these problems by reaching out to a variety of military offices to develop a system or mechanism to allow trainees to take advantage of this program. Thus, we concluded that these hurdles while unfortunate are beyond your control.

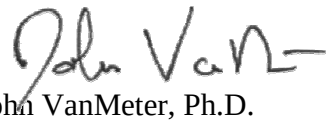
To date the program has had 2 trainees go through the training program. Our telephone interview with one of your trainees with Gerald York, M.D., confirmed our initial impression of your program. He was extremely enthusiastic about the program and described how the training has

given him the tools to transform his research from the case report model to prospective clinical research. Due to limitations on travel resulting from the sequester, he had to use his annual leave and pay for the travel himself to complete the training, a very strong testament to the extent to which he valued the program. He confirmed the difficulties related to attending the training.

The solutions we discussed were to try to incorporate distance-learning solutions, such as video conferencing with several onsite meetings per year that would be limited to long weekends. In addition, we suggested possibly having trainees assigned to the US Army Medical Research and Materiel Command at Ft. Detrick as a way to get release for the trainees from their commands and avoid additional service commitment. In this regard, Dr. Johnston contacted a program officer who has handled congressionally directed research from Ft. Detrick who will look into this type of administrative solution. Longer-term plans might include linking this training to the clinical investigation programs in the major medical centers across the United States.

In summary, we commend you for creating an excellent program providing training in the latest neuroimaging research techniques along with the essential methodologies for conducting clinical research including basics such study design and statistics. The BRAIN team has invested considerable effort to build a very impressive and broad-based mentoring program, channeling expertise from multiple disciplines in the fields of pediatric brain injury and advanced brain imaging. To date the DoD funding has served as the major catalyst in the development of this unique training program, which already benefits not only military trainees but also civilians who share in this experience with their DoD colleagues. Enormous effort and planning has gone into making this program a reality, which could not have happened without support of this grant. At this point consolidation of the BRAIN program is critical. We understand the impediments to recruiting trainees are beyond your control and laud your efforts to resolve these problems. We strongly recommend that the DoD continue to support this high caliber training program by the inclusion of civilian trainees while the program directors and DoD work toward solutions to the challenges currently facing military trainees.

Sincerely,



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Phone: (202) 687-3592 Fax: (202) 687-7906

BRAIN Seminars

Principles and Clinical Application of Advanced MRI
&
Basic Mechanisms of brain injury and recovery

Title	**Presenter**
Hazards and safety of MRI	Dr. Stanley Fricke
Introduction to MRI: Basic principles and methodologies	Dr. Stanley Fricke
Magnetic resonance spectroscopy	Dr. Stanley Fricke
Metabolic mapping of the pediatric brain	Dr. Stanley Fricke
Pulse sequences and quality control	Dr. Stanley Fricke
Pulse sequences and coil selection: Physics for physicians	Dr. Iordanis Evangelou
Coil operation and selection	Dr. Iordanis Evangelou
Conventional MRI: Strengths and limitations for detecting brain injury	Dr. Gilbert Vezina
Motion correction and high resolution reconstruction	Dr. Cedric Clouchoux
Mechanisms of brain injury in the preterm and term newborn	*Dr. Adre du Plessis*
MRI diagnosis of brain injury in the preterm and term infant	Dr. Jonathan Murnick
Advanced MRI techniques to interrogate brain injury in preterm and term infant	Dr. Catherine Limperopoulos
Mechanisms and MRI manifestations of stroke in childhood	*Dr. An Massaro*
Pediatric MRI without sedation: Is it the art or science?	Dr. Raymond Sze
Microstructural assessment of the injured brain: Diffusion weighted and tensor imaging	Dr. Carlo Pierpaoli
Strengths and limitations of diffusion MRI for investigating the brain in health and disease	Dr. Carlo Pierpaoli
Comparison of TORTOISE vs. DTI studio for diffusion imaging analysis	Dr. Carlo Pierpaoli
So many DTI data, so many software packages, so little time: A survival guide to DTI data processing	Dr. Carlo Pierpaoli
Normal and abnormal development of the cerebellum	*Dr. Adre du Plessis*
Normal and abnormal development of the posterior fossa structures	*Dr. Adre du Plessis*
Brain development in an adverse intrauterine milieu	*Dr. Catherine Limperopoulos*
Understanding normal brain development: Role of MRI	Dr. Gilbert Vezina
MRI diagnosis of normal and abnormal posterior fossa development	Dr. Gilbert Vezina
Spatio-temporal modeling and analysis of brain development in MRI	Dr. Ahmed Serag
Pediatric high resolution morphometric brain techniques	Dr. Cedric Clouchoux
3D Modeling of the brain	Dr. Cedric Clouchoux
Normal and abnormal regulation of cerebral blood flow and metabolism	*Dr. Adre du Plessis*
Quantification of cerebral perfusion: Where are we at?	Dr. Zarir Khademian

Perfusion imaging techniques for acquired brain injury	Dr. Zarir Khademian
'Static brain injury' in the newborn is an oxymoron	*Dr. Adre du Plessis*
Cerebellar injury and transtentorial diaschisis in development	*Dr. Catherine Limperopoulos*
Functional MRI and MRI hardware components	Dr. William Gaillard
fMRI principles and applications	Dr. William Gaillard
Resting functional connectivity: What is the physiologic basis and clinical application?	Dr. William Gaillard
A new era of fast and furious MRI	Dr. Nadja Kadom
Measuring fMRI differences: lessons from epilepsy populations	Dr. Stanley Fricke
Basic principles of fMRI, paradigm design, and image analysis	Dr. Madison Berl
Measuring drug induced changes in brain function in resting-state	Dr. William Gaillard
	Dr. Najmeh Mahani
Mechanisms and manifestations of traumatic brain injury	*Dr. Gerald Gioia*
Assessing neuropsychological outcome after brain injury in childhood	*Dr. Gerald Gioia*
MRI in the diagnosis and timing of traumatic brain injury	Dr. Gilbert Vezina
Novel susceptibility weighted imaging techniques and their emerging role in pediatric brain injury	Dr. Iordanis Evangelou
LC model and quantification of metabolic disturbances following brain injury	Dr. Stanley Fricke

Example of a Medical-based Online Learning Portal

JEFF M. SESTOKAS
Senior Instructional Systems Technologist /Research Scientist
144 Michigan Ave NW, WW3.5-701-A
Washington, D.C. 20010
202-476-3246

Professional Experience Summary

Specializing in instructional design, education research, and technology development, my interests include the application and diffusion of instructional technologies to military personnel and corporate firms. For several years I have worked on projects developing training for complex organizations and military command environments with a focus on designing classroom materials, scenarios, evaluation instruments, and assessment tools within computerized and live environments. Additionally, I have served as a program manager and core team member on various projects including developing an intelligent mentoring system for future JFACCs of the United States Air Force, designing nuclear training programs for the Air Force Inspection Agency, Air Force Nuclear Security Forces Center, and Nuclear Weapons Center. Also, I have developed classroom and web-based training programs for the Army Research Institute, Army National Guard Bureau, and the Department of Homeland Security by using knowledge elicitation and analysis methods such as Cognitive and Behavioral Task Analysis to understand the expertise of emergency first responders, submarine commanders, crude unit operators, nuclear surety inspectors, human terrain teams, company intelligence support teams, and master gunners.

Job Assignments

PROFESSIONAL EXPERIENCE

Children's National Medical Center - Washington D.C. **2012-Present**
Senior Research Scientist/Instructional Systems Designer

- Leader for the Medial Education department's instructional design and technology initiatives including custom online and mobile learning portals, computerized training modules, and technology-based plugins.
- Primary contributing member to several medical research and training development projects.

Engineering & Computer Simulations - Washington D.C. **2010-2012**
Senior Research Scientist/Instructional Systems Designer

- Group Leader for the Cognitive Training Group based in Washington D.C.
- Program Manager for a $1 million effort developing simulation training for use in the FEMA Qualification System (FQS) to certify and credential 50,000 federal emergency management and response employees.
- Primary contributing member to several research and training development projects for the Center for Disease Control, Training Support Working Group, National Guard Bureau, Department of Homeland Security, National Science of Academies, and the Naval Air Warfare Center.
- Authored and coauthored several publications on topics relating to Instructional Design and Technology.

Applied Research Associates Inc. - Washington D.C. **2006-2010**

Senior Scientist II

- Served as a core team member on various projects including developing an intelligent mentoring system for future JFACCs of the United States Air Force, designing nuclear training programs for the Air Force Inspection Agency, Air Force Nuclear Security Forces Center, and Nuclear Weapons Center.
- Developed classroom and web-based training programs for the Army Research Institute, Army National Guard Bureau, and the Department of Homeland Security by using analysis methods such as Cognitive and Behavioral Task Analysis to understand the expertise of emergency first responders, submarine commanders, crude unit operators, nuclear surety inspectors, human terrain teams, company intelligence support teams, and master gunners

Baldwin-Wallace College - Berea, Ohio **2004-2006**

Adjunct Instructor

- Developed and taught courses for the Public Relations major including Public Relations Writing, PR Technology, Studies in Public Relations, and Persuasive Campaigns.
- Created curriculum and assessments that adhere toward the educational goals and objectives set forth by Baldwin-Wallace College and The Council for Higher Education Accreditation.
- Wrote several proposals to develop a new multimedia technology lab for P.R. and Communications majors.

Education/Security Clearance

M.A. Ed.	Instructional Technology (Focus in Instructional Design and Technology)	Baldwin-Wallace College Berea, OH
B.A.	English (Integrated Language Arts Education)	Baldwin-Wallace College Berea, OH

Security Clearance Level: Top Secret

Awards

ARA Technical Publication Award - *An Adaptive Learning Architecture for the Next Generation Simulation Training Systems*. 2009.

ARA Team Player of the Year Award Nominee – *Effort to Improve the Air Force Nuclear Enterprise*. 2009.

ARA Technical Publication Award - *High-Fidelity Simulation/Mentor System for General Officers in High-Stakes Operational Environments*. 2007.

Project Management Certification, 2007.

B-W IABC Teaching Award for Excellence, (Public Relations Technology) 2006
B-W IABC Teaching Award for Diversity & Innovation, (Discover Puerto) 2004

Selected Publications and Presentations

Sestokas, J. M. (2011). Design Framework for Mapping Pedagogical Requirements within Advanced Training Systems. Paper submitted to the Interservice/Industry Training, Simulation, and Education Conference, Orlando, FL.

Sestokas, J. M., & Pigora, M. (2011). Command-Level Decision Making for Transit Emergency Managers (Interim Report prepared under Contract TCRP A-36; Contract for Transit Cooperative Research Program (TCRP) Transportation Research Board of the National Academies). Washington D.C.: Engineering and Computer Simulations, Inc.

Veinott, E., Sestokas, J. M., Zimmerman, L.A., Bell, J., Manning. D. (2011). *Developing Remote Training Tools for Company Intelligence Teams*. Paper accepted to the Interservice/Industry Training, Simulation, and Education Conference, Orlando, FL

Sestokas, J. M., Trapp, M., & Randall, G. (2010). The Nuclear Security Inspection Course (Final Report prepared under Contract GS-10F-0298K, Order No. GSA RFQ 401368; Contract for U.S. Air Force Security Forces Center, Lackland AFB, TX). Fairborn, OH: Klein Associates Division of Applied Research Associates.

Zimmerman, L. A., Sestokas, J. M., Burns, C. A., Grover, J., Topaz, D. & Bell, J. (2010). Improving Attrition Rates in the M1A1/M1A2 Master Gunner Course (Final Report prepared under Subcontract ARI-ARA-07-001, Task Order 14524 (DRC); Contract # W74V8H-04-D-0048 for U.S. Army Research Institute for the Behavioral and Social Sciences, Fort Knox, KY). Fairborn, OH: Klein Associates Division of Applied Research Associates.

Veinott, E., Sestokas, J. M., Zimmerman, L.A., Bell, J., Manning. D. (2010). Home Station Training Tools for Company Intelligence Support Teams (Final Report prepared under Contract # W91WAW-09-R-0080 for U.S. Army Research Institute for the Behavioral and Social Sciences, Fort Knox, KY). Fairborn, OH: Klein Associates Division of Applied Research Associates.

Zimmerman, L. A., Sestokas, J. M., & Burns, C. A. (2010). Using High Fidelity Computerized Training to Prepare Commanders for Operational Decision Making. In K.L. Mosier & U. M. Fischer (Eds), *Informed by Knowledge: Expert Performance in Complex Situations.*

Zimmerman, L. A., Sestokas, J. M., Sanders, W., Bell, J., & Manning, D. (2009). Training methods to build human terrain mapping skills (Final Report prepared under Subcontract ARI-ARA-07-001 (DRC); Contract # W74V8H-04-D-0048/0023 for U.S. Army Research Institute for the Behavioral and Social Sciences, Fort Knox, KY). Fairborn, OH: Klein Associates Division of Applied Research Associates.

Sestokas, J.M., Burns, C.A., & Worth, T.F. (2009). *An Adaptive Learning Architecture for Next Generation Simulation Training Systems*. Paper accepted to the Interservice/Industry Training, Simulation, and Education Conference, Orlando, FL

Sestokas, J.M. & Burns, C.A. (2009). Evaluating Nuclear Surety Inspector's Course (Final Report prepared under Contract # FA4819-07-D-0001 for Air Force Inspection Agency/Albuquerque, NM.). Fairborn, OH: Klein Associates, A Division of Applied Research Associates.

Zimmerman, L. A., Burns, C. A., & Sestokas, J. M. (2009). High-fidelity simulation/mentoring system for General Officers in high-stakes operational environments. *ARA Technology Review, 5,* 29-36.

Sestokas, J. M., (2009). Technology Training Standards for the First Responder Community [Presentation to the InterAgency Board in Washington, D.C.]. Fairborn, OH: Klein Associates, A Division of Applied Research Associates.

Zimmerman, L. A., Sestokas, J. M., Sanders, W., Bell, J., & Manning, D. (2009). Training

methods to build human terrain mapping skills (Final Report prepared under Subcontract ARI-ARA-07-001 (DRC); Contract # W74V8H-04-D-0048/0023 for U.S. Army Research Institute for the Behavioral and Social Sciences, Fort Knox, KY). Fairborn, OH: Klein Associates Division of Applied Research Associates.

Sestokas, J. M., (2008). Cognitively Authentic Simulation Training for the First Responder Community [Presentation to the InterAgency Board in Ft. Lauderdale, FL]. Fairborn, OH: Klein Associates, A Division of Applied Research Associates.

Zimmerman, L.A., Sestokas, J.M., & Bongiorno (2008). *The Worst that can Happen: Creating Realistic Emergency Management Scenarios*. Paper accepted to the Interservice/Industry Training, Simulation, and Education Conference, Orlando, FL

Zimmerman, L. A., Sestokas, J. M., & Burns, C. A. (2008). Living in the hot seat: Mentoring software to support JFACC performance (Final Report prepared under Contract # FA8750-05-C-0077 for AFRL/IFSA, Rome, NY.). Fairborn, OH: Klein Associates, A Division of Applied Research Associates.

Sestokas, J.M. & Burns, C.A. (2008). Evaluating Nuclear Weapons Center Certification Process Course (Final Report prepared under Contract #FA4819-07-D-0001 for Nuclear Weapons Center/Albuquerque, NM.). Fairborn, OH: Klein Associates, A Division of Applied Research Associates.

Sestokas, J.M. & Hutton, R.J.B. (2008). Supporting the Development of a DSTA In-House CSE Capability: Designing for Sensemaking Workshops (Final Report prepared under Contract # POD 0613613 SoW B for Defense Science & Technology Agency.). Fairborn, OH: Klein Associates, A Division of Applied Research Associates.

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Zimmerman, L., Burns, C., & Sestokas, J.M. (2007). *High-Fidelity Simulation/Mentor System for General Officers in High-Stakes Operational Environments.* Paper accepted to the Interservice/Industry Training, Simulation, and Education Conference, Orlando, FL

Harris-Thompson, D., Long, W. G., O'Dea, A., Gabbard, S. R., & Sestokas, J. M. (2007). *Center for Operator Performance Pilot Study: The nature of expertise in the control of continuous processes* (Final Report submitted to Center for Operator Performance c/o Beville Engineering, Inc., Dayton, OH). Fairborn, OH: Klein Associates Division, Applied Research Associates.

Sestokas, J. M., & Zimmerman, L. (2007). *The importance of high-fidelity computer training for commanders in high stakes operational environments*: Poster session to be presented at the 8th International Conference on Naturalistic Decision Making, Monterey, CA.

Sestokas, J. M., & Gilmore, S. (2005, April 2). *Discover Puerto Rico: Interactive education telecollaborative/documentary*, Gund Arena, Cleveland, OH.

Hoffland, R., Leblanc, W., & Sestokas, J. M. (2004). *Teacher retention research study 2004: A qualitative/quantitative grounded theory examining the factors that contribute to a secondary teacher's longevity in the classroom* (Research paper). Berea, OH: Baldwin-Wallace College.

Five-step design approach for developing the online BRAIN courseware

	Learner's Abilities	Instructional Methods	Instructional Content	Assessment Methods
Define and organize the knowledge and skill components of each instructional module in a sequence from basic to complex learning units.	Account for the learner's prior knowledge and skill development.	Establishes the approach for presenting the instructional content.	Focuses on the tasks and information related to the teaching concept(s) or topic(s).	Focuses on designing methods for assessing learning and long-term content mastery.